II. REMARKS

By the foregoing amendment, the applicants have canceled claims 1-31 without prejudice and introduced new claims 32-66. **In view of the notice, the undersigned assumes that applicants' amendment filed August 9, 2005, has not been entered. Therefore, the present amendment is based upon the assumption.**

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Claims 32-48 and 50-64 are directed to the same subject matter as originally filed claims 1-31, and thus also find support in the original claims as well. As a convenience to the examiner, the applicants have provided a table (see Appendix) that sets forth the concordance between the canceled claims and the newly presented claims.

The applicant submits that new claims 34 and 43 are slightly different than their respective originally derived claims (*i.e.*, claims 2 and 12). Specifically, new claim 34 is directed to a method as claimed in claim 33 wherein the **infectious agent** is a viral vector containing therapeutic genetic material. The term "infectious agent" finds proper antecedent basis from claim 33. Support for claim 34 can be found in originally filed claim 2 as indicated by the table above.

New claim 43 is directed to a polymer modified element according to claim 41 wherein the polymer backbone is based upon monomer units such as N-2 hydroxypropylmethacrylamide (HPMA), N-(2-Hydroxy ethyl)-L-Glutamine (HEG), ethyleneglycol-oligopeptide, **or dextran**. The term "dextran" is supported in Example 17 of the specification and by our arguments on page 10 of our response filed August 9, 2005 regarding WO 98/19710.

New claim 51 is directed to a polymer modified biological element according to claim 50 wherein said antibody and antibody fragments are monoclonal. Support for new claim 51 can be found throughout the specification, for example, originally filed claim 17 and lines 9-12 on page 9.

New claim 65 is directed to a method according to claim 34, wherein the synthetic hydrophilic multivalent polymer comprises a polymer backbone based upon monomer units selected from the group consisting of N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-1-glutamine (HEG), ethyleneglycol-oligopeptide, or dextran. Support for new claim 65 can be found throughout the specification, for example, on page 6, lines 25 to 30 as well as the content of WO 98/19710, which is included in the applicants' invention by reference.

New claim 66 is directed to a polymer modified biological element as claimed in claim 6 wherein the biological element is an adenovirus. Support for new claim 66 can be found throughout the specification, for example, on page 13, lines 18-21 and Example 4.

On page of the official action, the examiner objected to claims 4, 10-24, and 36-31 under 37 C.F.R. § 1.75(c) as being in improper form due to multiple dependent claims depending from other multiple dependent claims. In view of the foregoing amendment, the objection of claims 4, 10-24 and 26-31 is moot. The applicants submit that the multiple dependencies are not present in new claims 32-66 as set forth above. Accordingly, the applicants respectfully request that the objection to claims 4, 10-24 and 26-31 has been overcome, and should now be removed.

On pages 2 and 3 of the official action, the examiner objected to claim 25 under 37 C.F.R. § 1.75(c) as being an improper dependent claim because it failed to limit the subject matter of the previous claim. As discussed above, claim 25 has been canceled without prejudice.

Rejection Pursuant to 35 U.S.C. §112, First Paragraph

Written Description

On pages 3-5 of the official action dated August 9, 2005, the examiner rejected claims 1-3, and 5-9 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the examiner asserted that these claims encompass a broad genus of multivalent polymers that include any multivalent polymer of any type. The examiner further alleged that these multivalent polymers retain the function of forming a complex with any type of bacterial cell, viral particle, bacteriophage, or spore wherein the multivalent polymer forms at least two covalent linkages and alters at least one

biological or physiochemical property of the biological element. The examiner further asserted that the specification teaches only two working examples around multivalent polymers having an N-2-hydroxypropylmethylacrylamide (hereafter "HPMA"), N-(2-hydroxyethyl)-1-glutamine (hereafter "HEG"), or ethylenglycol-oligopeptide backbone. The examiner finally alleged that no additional multivalent polymer that form multiple covalent linkages per polymer molecule to modify biological properties of a bacterial cell, viral particle, bacteriophage or spore are described in the specification or in the prior art. The examiner concluded that given the enormous genus of multivalent polymerse, the lack of description in the specification or prior art of other embodiments of such multivalent polymers, one of skill would reasonably conclude that the applicants were not in possession of the broadly claimed invention.

As discussed above, although claims 1-3 and 5-9 have been canceled such claims correspond to new claims 32-34 and 36-40. New claim 32 is directed to a method of modifying the biological and/or physicochemical properties of a biological element, said method comprising reacting said biological element with a synthetic hydrophilic multivalent polymer having multiple reactive groups wherein the biological element is linked to the polymer by a plurality of linkages. New claim 37 is directed to a polymer modified biological element in which the biological element is covalently linked to a synthetic hydrophilic multivalent polymer having multiple reactive groups wherein said polymer is linked to the biological element by at least two covalent linkages. Support for new claims 32 and 37 can be found throughout the specification, for example, on page 6, lines 13-15. The applicants respectfully submit that examples of a number of the synthetic hydrophilic mulivalent polymer backbones (i.e., HPMA, HEG and ethyleneglycol-oligopeptide) are fully described in specification for example, on page 6, lines 30-35 and Example 1. The applicants submit that the description of the examples using HPMA, HEG, and PEG provide sufficient guidance to other suitable polymers. One of skill in the art will know the chemical nature of the groups present on the surface of a biological element to couple with synthetic hydrophilic polymers. Using his knowledge of chemistry regarding reacting the polymer, one of skill can choose the necessary hydrophilic group required to be present on the polymer in order to transform the hydrophilic polymer into reactive groups which complement the surface of the biological element. Therefore, given the constraints on the system in terms of complementary reactive groups between the polymer and the biological element, one of skill, reading the description of the application, would be able to identify a limited number of

suitable hydrophilic multivalent polymers for manipulation. Thus, the applicants submit that they were in possession of the broadly claimed invention at the time of filing.

Dependent claims 33, 34, 36, and 38-40 depend from and contain the same limitation as new claim 32 or claim 37. Similarly, claims 35 and 41-48, 50-64 depend from and contain the same limitation. In view of the foregoing remarks and amendment, the applicants submit that the rejection of claims 1-3 and 5-9 under 35 U.S.C. §112, first paragraph, for lack of written description is moot, and a rejection of new claims 32-34 and 36-40 upon the same basis would be improper.

Enablement

On pages 5-8 of the official action, the examiner rejected claims 1-3 and 5-9 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the examiner asserted that while the embodiments of a multivalent polymer backbone consisting of either HPMA, HEG, or ethyleneglycol-oligopeptide are enabled by the specification, the specification does not provide a sufficient enabling disclosure wherein the mulivalent polymer is derived from a different polymer backbone. The examiner asserted that the nature of the invention is complex involving covalent attachment of a single polymeric molecule to at least two sites on the surface of an altered biological element (e.g., phage, virus, or bacterial cell). The examiner alleged that the breadth of the claims encompass a large number of multivalent polymers linked to these altered biological elements. The examiner further asserted that there is no significant guidance of other multivalent polymers wherein the backbone is not derived from HPMA, HEG, or ethyleneglycol-oligopeptide. The examiner alleged that using multivalent polymers to generate altered biological elements through multiple covalent linkages per polymer is novel in the art. The examiner cited WO 98/44143 as prior art that fails to provide further guidance with regard to adapting other types of polymer backbones for use in attaching biological elements to multivalent polymers with at least two covalent bonds.[1] The examiner concluded that due to these factors, one of skill in the art would have to perform undue trial and error experimentation to develop other types of multivalent polymers to practice the claimed invention.

[1] The examiner asserted that WO 98/44143 only teaches modifying a virus particle through a single covalent linkage with polyethylene glycol (PEG).

The applicants submits that the specification (and its teachings) clearly enables one of skill in the art to identify other hydrophilic multivalent polymer backbones other than HPMA, HEG, and ethyleneglycol-oligopeptide. The polymer backbone must be hydrophilic. The reactive groups that make up the hydrophilic backbone must complement those surface reactive groups on the surface of the biological element. The options available to one of skill in the art is limited to a finite number of combinations. The examples teach that using HPMA, HEG, and PEG demonstrate the types of reactive groups are required suitable for the polymer to form a linkage on the surface of the biological element. One of skill has this knowledge of this type of chemistry based upon the teachings of the specification. For example, the applicants submits that the fully included reference WO 98/19710 refers to the use of dextran as a hydrophilic multivalent polymer (see Example 17 of WO 98/19710). In addition to the disclosed examples of HPMA, HEG, and PEG, polysaccherides such as dextran could be identified by one of skill in the art to be a suitable hydrophilic multivalent polymer for reacting with particular surface molecules of a biological element. Accordingly, one of skill is initially directed to a particular area of suitable multivalent hydrophilic multivalent polymers for manipulation such that undue trial and error experimentation is not necessary.

As discussed above, dependent claims 33, 34, 36 and 38-40 depend from and contain the same limitation as new claim 32 or claim 37. Similarly, claims 35 and 41-48 and 50-64 depend from and contain the same limitation. In view of the foregoing remarks and amendment, the applicant submits that the rejection of claims 1-3 and 5-9 under 35 U.S.C. §112, first paragraph, for lack of enablement is moot and a rejection of new claims 32-34 and 36-40 upon the same basis would be improper.

Rejection Pursuant to 35 U.S.C. §112, Second Paragraph, Indefiniteness

On page 8 of the official action dated August 9, 2005, the examiner rejected claims 1-3 and 5 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Specifically, the examiner asserted that claim 1 was unclear with regard to the phrasing "change or modify" because it appeared to him as being synonymous. The examiner further alleged that claim 3 was unclear for the phrasing "such as" because it was unclear whether the limitation following this phrase are a necessary part of the claim.

In view of the foregoing amendment, the rejection of claims 1-3 and 5 is moot. The applicants submit that the term "such as" is not present in claim 32 or 33. Accordingly, the rejection of claims 1-3 and 5 under 35 U.S.C. §112, second paragraph is moot and a rejection of new claims 32 and 33 upon the same basis would be improper.

III. CONCLUSION

In view of the foregoing, the applicants request entry of the enclosed amendment prior to further substantive examination on the merits. . Should the examiner have any questions or comments regarding this response or the application, the examiner is urged to contact the undersigned at the number indicated.

Respectfully submitted,

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